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Declaration under Rule 4.17:

— *of inventorship (Rule 4.17(iv)) for US only*

Published:

— *with international search report*  
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(54) Title: METHOD FOR THE DIAGNOSIS AND TREATMENT OF VASCULAR DISEASE

(57) Abstract: A method for diagnosing decreased vascular function is disclosed. The method includes assaying the number of endothelial progenitor cells. A method for detecting increased cardiovascular risk is also disclosed, as is a method diagnosing atherosclerosis. In one example, the methods include assaying the number of endothelial progenitor cells. A method for treating a subject with decreased vascular function is disclosed. The method includes administering a therapeutically effective amount of endothelial progenitor cells to the subject. In one embodiment, the subject has atherosclerosis.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/36317

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 49/00; A01N 63/00; C12P 21/06; C12N 5/00, 15/00, 15/63  
 US CL : 424/9.2; 93.1, 93.2, 93.21; 435/69.1, 320.1, 325, 455; 514/44

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
 U.S. : 424/9.2; 93.1, 93.2, 93.21; 435/69.1, 320.1, 325, 455; 514/44

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  
 none

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
 Please See Continuation Sheet

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EIZAWA T. et al. Circulating endothelial progenitor cells are reduced in hemodialysis patients. Current Medical Research Opinion. 2003, Vol. 19, No. 7, pages 627-633, see entire document.	1-21, 23-53
Y	VASA M. et al. Number and migratory activity of circulating endothelial progenitor cells inversely correlate with risk factors for coronary artery disease. Circulation Research. July 2001. Vol. 89, pages e1-e7, see entire document.	1-21, 23-53
Y	VASA M. et al. Increase in circulating endothelial progenitor cells by statin therapy in patients with stable coronary artery disease. Circulation. June 2001, Vol. 103, pages 2885-2890, see entire document.	1-21, 23-53
P,Y	HILL J.M. et al. Circulating endothelial progenitor cells, vascular function, and cardiovascular risk. New England Journal of Medicine. February 2003. Vol. 348, No.7, pages 593-600, see entire document.	1-21, 23-53
Y	SHINTANI S. et al. Mobilization of endothelial progenitor cells in patients with acute myocardial infarction. Circulation. 2001. Vol. 103, pages 2776-2779, see entire document.	1-21, 23-53

Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier application or patent published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means		
"P" document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

05 August 2004 (05.08.2004)

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INTERNATIONAL SEARCH REPORT

C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KALKA C. et al. Vascular endothelial growth factor(165) gene transfer augments circulating endothelial progenitor cells in human subjects. Circulation Research. June 2000, Vol. 86, pages 1198-1202, see entire document.	20
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Y		21, 23-29
A	BAHLMANN F.H. et al. Erythropoietin regulates endothelial progenitor cells. Blood. February 2004, Vol. 103, No. 3, pages 921-926, see entire document.	20-21, 23-29

**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US03/36317

**Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)**

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claim Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claim Nos.: 22 because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:  
Claim 22 is unsearchable because this claim improperly depends upon itself.
  
3.  Claim Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
  
4.  No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

  

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

PCT/US03/36317

**Continuation of B. FIELDS SEARCHED Item 3:**

Databases: STN:medline, scisearch, caplus, cancerlit, EAST:USPTO, JPO, EPO, Derwent.

Search terms: Endothelial progenitor cells, VEGFR, CD32, blood sample, Cholestrol, Vascular, Cardiovascular, isolation, diagnostic, therapeutic, therapy.